UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,753	07/25/2007	Henrik Arnberg	15665-010US1	3748

26191 7590 12/23/2008
FISH & RICHARDSON P.C.
PO BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
CHANDRA, GYAN	
ART UNIT	PAPER NUMBER
1646	

NOTIFICATION DATE	DELIVERY MODE
12/23/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/599,753	ARNBERG, HENRIK	
	Examiner	Art Unit	
	GYAN CHANDRA	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-18,21-27 and 29-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-18,21-27 and 29-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/7/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 11/07/2008 is acknowledged and fully considered.

Status of Application, Amendments, And/Or Claims

The amendments of claims 16, 22, 27 and 29, and the addition of claims 30-31 have been made of record.

Claims 16-18, 21-27 and 29-31 are pending and under examination.

Information Disclosure Statement

The Information Disclosure Statement (IDS) submitted on 11/07/2008 has been considered.

Response to Arguments

Claim Objections/Rejections – *withdrawn*

Claim objection

The objection of claims 16, 22 and 27 for reciting the word "the" before "GM-CSF" is withdrawn in view of Applicants' deletion of the word "the" before GCSF.

Claim Rejections - 35 USC § 102- *withdrawn*

The rejection of claims 16, 21-27 and 29 under 35 U.S.C. 102(b) as being anticipated by Grabstein et al is withdrawn in view of Applicants' amendments to claim 16 which now is drawn to treating a localized bacterial infection comprising local administration of GM-CSF polypeptide. However, upon further consideration a new ground of rejection is applied in view of Applicants amendments of the instant claims.

Claim Rejections - 35 USC § 103*- withdrawn*

The rejection of claims 17 and 18 under 35 U.S.C. 103(a) as being unpatentable over Grabstein et al in view of Sampathkumar is withdrawn in view Applicants' amendment of claim 16 as discussed above (see Claim Rejection 35 USC 102- withdrawn). However, upon further consideration a new ground of rejection is applied in view of Applicants amendments of the instant claims.

Claim Rejections - 35 USC § 112-*written description*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 16-18, 21-26 and 29 are withdrawn in view of Applicants amendment of claim 16 to delete the term "fragment or derivative". However, Claim 27 remains rejected and newly filed claim 31-32 are now rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons of record in pg. 3-6 of the Office Action of 8/7/2008 because claims 27, 30 and 31 recite the term "a fragment or derivative".

Applicants argue (pg. 5-6 of Response) that derivatives of GM-CSF are well known in the art and provides a reference by Knosli et al (1992) that the pegylated GM-CSF is biologically active.

Applicants' arguments have been fully considered but they are not persuasive because the specification does not define that defined the term "GM-CSF derivative" as a pegylated GM-CSF. The term "derivative" is drawn to any

alteration or chemical derivative of the instant polypeptide and therefore, the term is not limited to only pegylation of the polypeptide. One of the skill in the art would not know that the a derivative of GM-CSF is only pegylated GM-CSF and therefore, applicants are not in possession of the invention as it is drawn to a method of treating a mammal suffering from any localized bacterial infection by administering any GM-CSF fragment or derivative.

Claim Rejections - 35 USC § 112-*enablement*

Claims 16-18, 21-27 and 29 remain rejected and newly filed claims 30-31 are now rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a mammal suffering from gingivitis comprising administering therapeutically effective amount of GM-CSF, does not reasonably provide enablement for treating any bacterial-related disease by administering a composition comprising GM-CSF, a fragment or derivative thereof.

Applicants argue (see pg. 11/7/2008 of Response) that they have deleted the term "fragments and derivative" from claim 16 and that other claims e.g., 27, 30 and 31 are drawn to a derivative which is well know in the art such as PEG-modified GM-CSF. Applicants argue that claim 16 is amended to recite a method for treating a localized bacterial infection or a bacterial-related disease, or both comprising locally administering a therapeutically effective amount of a GM-CSF. Applicants' arguments have been fully considered but they are not persuasive because claims 27, 30 and 31 require a derivative or fragment of GM-CSF which

can treat any localized bacterial infection by administering said derivative or fragment of GM-CSF. Additionally, claims 16-18, 21-27, 29 were rejected because specification does not disclose how one of the skill in the art can treat any localized bacterial infection. The specification only teaches treating periodontal diseases by locally administering GM-CSF polypeptide. The art teaches that periodontal disease surface as a result of weak immunological response against bacterial infections. It is not clear how one of the skill in the art can treat a localized bacterial infection when it occurs in an internal organ such as heart, brain, lung or liver by administering a fragment, derivative of GM-CSF or even the polypeptide GM-CSF. The specification provides enablement only for a method for treating gingivitis or localized periodontal diseases but the specification does not enable one of the skill in the art to make and/or use the claimed invention in its full scope.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 30, the phrase "essentially the function and activity" renders the claim(s) indefinite because the claim(s) include(s) elements not actually disclosed (those encompassed by "essentially the function and activity

"), thereby rendering the scope of the claim(s) unascertainable. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

For the purpose of comparing the claims with the prior art, it is noted that the specification does not specifically define “essentially the function and activity of the GM-CSF.” Therefore, in claim 30, the limitation to the extent it reads on treating a bacterial infection.

Claims 16, 21-27 and 29-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grabstein et al (US Patent No. 5,162,111) in view of Grzybowski et al (Int. J. Pharmaceutics 184: 179-187, 1999).

The instant claims are broadly drawn to a method of treating a mammal suffering from a localized bacterial infection, a bacterial-related disease or both

comprising locally administering a therapeutically effective amount of a composition comprising at least one GM-CSF polypeptide (16, 29), wherein composition is suitable for administration via injection (claim 21), wherein said GM-CSF or fragment or derivative thereof is present in the composition in a unit dosage amount of 5 µg to 800 µg (claim 22), wherein the unit dosage amount is 50 µg to 100 µg (claim 23), wherein said composition is administered at intervals ranging from once a day to once every third week (claim 24), wherein said composition is administered a total of 1 to 3 times for a period of one week (claim 25), wherein said composition comprises a therapeutically effective amount of at least one other active ingredient (claim 26), and wherein said GM-CSF or fragment or derivative thereof is produced by means of a recombinant expression system (claim 27); and wherein the composition comprises at least one derivative or a GM-CSF polypeptide having essentially the function and activity of the GM-CSF (30, 31).

Grabstein et al teach a composition comprising GM-CSF for the treatment of bacterial infection (col. 11, lines 50+, Example 1 and claim 1). Grabstein et al teach making GM-CSF using recombinant technology (col. 8, lines 18+, Example 5 and claim 2). They teach that GM-CSF is efficacious as an anti-infective agent (col. 4, lines 35+). They teach administering a recombinant GM-CSF to a subject suffering from bacterial infection in dosages of about 0.05 to 500 ug/Kg of body wt of the subject per day (col. 5, lines18+ and Examples 1-2, and 4) or periodically as contemplated in claim 8, which would be equivalent to 30 µg to 30,000 µg for a 60 Kg subject, and thus the teachings of Grabstein et al meet the

limitations of claims 22-26. Grabstein et al teach a composition comprising aqueous solution suitable for intravenous, intramuscular, subcutaneous or peritoneal injection (col. 5, lines 44+ and claims 4-5). They teach administering GM-CSF in a single or multiple doses (col. 5, line 26). Grabstein et al teach that some variation in dosage will occur depending upon the condition of the subject being treated (col. 5, lines 20+). Grabstein et al do not teach locally administering GM-CSF for treating a local bacterial infection.

Grzybowski et al do teach among the many factors to date tested G-CSF and GM-CSF are the most powerful stimulators of wound repair (page 180, left column). Grzybowski et al do teach preparing dressings containing GM-CSF or G-CSF which is suitable for local administration (page 180, Materials and methods). Grzybowski et al do teach that the art discloses a method for using GM-CSF for treating bacterial infection (see Grabstein et al as applied above, and Schneider and Dschner, Clin. Micorobiol. Infect. 4: 119-122, 1998). It is noted that the reference Schneider and Dschner is applied to support the state of the art and not as a prior art.

Therefore, it would have been prima facie obvious to one of the skill in the art to use dressings comprising GM-CSF for locally administering GM-CSF for treating a local bacterial infection as taught by Grzybowski et al. One of the skill in the art would have been motivated to use such dressings comprising GM-CSF for treating a localized bacterial infection because Grzbowski et al teach that such dressings efficiently deliver GM-CSF (as measured on page 183, left column). One of the skill in the art would have a reasonable success in locally

administering a composition comprising GM-CSF for treating a bacterial infection because Grzbowski et al teach a dressing that comprises GM-CSF for the local administration of GM-CSF.

Claims 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grabstein et al in view of Grzbowski et al as applied to claims 16, 21-27 and 29-31 above, and further in view of Sampathkumar (US Patent No. 4,804,530).

The instant claims are further drawn to a method of treating a mammal suffering from a localized bacterial infection, a bacterial-related disease or both comprising locally administering a therapeutically effective amount of a composition comprising at least one GM-CSF polypeptide, wherein the bacterial infection or bacterial-related disease is selected from periodontal disease or sinusitis (claim 17), and wherein the periodontal disease is gingivitis or periodontitis.

The teachings of Grabstein et al in view of Grzbowski et al are summarized as set forth supra. Neither Grabstein et al nor Grzbowski et al teach treating a localized bacterial infection or bacterial related disease selected from periodontal or sinusitis and wherein periodontal disease is gingivitis or periodontitis.

Sampathkumar does teach diseases such as periodontal disease involves bacterial infection (col. 1, lines 27+). Sampathkumar teaches that periodontal diseases affect the periodontum, which is the investing and supporting tissue surrounding a tooth). Sampathkumar teaches that gingivitis and periodontitis are

inflammatory disorders of gingiva and the periodontal ligaments, respectively. Sampathkumar teaches that oral cavity diseases which include gingivitis and periodontitis are initiated/and or perpetuated by bacteria in the oral cavity (col. 37+).

Thus, it would have been obvious to one ordinary skilled in the art at the time the instant invention was made to modify the invention of Grabstein in view of Grzbowski et al who teach the treatment of bacterial disease using locally adminstering GM-CSF to incorporate the treatment of gingivitis using the GM-CSF in view of Sampathkumar who teaches the gingivitis is localized bacterial disease as GM-CSF is known to elicit antibacterial effects. One would have been motivated to do so to because gingivitis is known to be a bacterial disease. One would have a reasonable expectation of success in treating a local bacterial disease by locally administering GM-CSF, since the treatment of bacterial diseases by administering the GM-CSF to a subject has been known in the art at time the instant invention was made.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GYAN CHANDRA whose telephone number is (571)272-2922. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gyan Chandra
Art Unit 1646
08 December 2008
Fax: 571-273-2922

/Robert Landsman/
Primary Examiner, Art Unit 1647